CASE REPORTS

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Herpes Type 2 Meningitis Following Herpes Progenitalis

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CULTURE OF herpesvirus hominis type 2 from cerebrospinal fluid of adult patients with aseptic meningitis has been reported sporadically.[1-3] Herpesvirus hominis type 2 infections of the central nervous system in association with herpes progenitalis have also been observed but more rarely.[4,5] A case of herpesvirus hominis type 2 meningitis after herpes progenitalis is reported in which the cerebrospinal fluid level of protein is the highest reported to date.

Report of a Case

A 28-year-old woman was admitted to Moffitt Hospital on October 13, 1974 because of sudden onset of severe low back pain without dysuria, followed by headache, fever, shaking chills, meningismus, ocular pain on downward gaze and lethargy. Three days previously, vesicular vulvar lesions developed and were diagnosed by a gynecologist as genital herpes; a single application of neutral red with photo inactivation was associated with symptomatic relief. The patient had no history of herpes infection but had been exposed to culture-proved tuberculosis two months earlier.

On physical examination temperature was 40°C (104°F), blood pressure 110/68 mm of mercury and pulse 120 per minute. Pertinent findings included bilateral tender inguinal adenopathy, multiple crusted vulvar lesions on erythematous bases with a normal appearing cervix and meningismus with positive Brudzinski's and Kernig's signs. There was no tenderness in the costovertebral angle, no skin or oral lesions, no ocular lesions and no abnormalities in sensory, motor and cerebellar function. Cranial nerves were intact. Laboratory data included a leukocyte count of 8,300 per cu mm with 75 percent polymorphonuclear cells, 15 percent lymphocytes and 10 percent monocytes; hematocrit 42 percent; sedimentation rate 13, and normal levels of serum electrolytes, creatinine and blood urea nitrogen. Results of urinalysis were within normal limits, and Venereal Disease Research Laboratories (VDRL) and purified protein derivative (PPD, intermediate strength), and mumps skin tests gave negative results. Roentgenograms of chest, skull, sinuses, cervical spine and lumbosacral spine showed no abnormalities.

Admission lumbar puncture was carried out and the cerebrospinal fluid showed leukocytosis (mostly lymphocytes), elevated protein and borderline glucose levels (Table 1). Because of these values and the patient's rigors, intravenous ampicillin therapy was started, pending routine culture results. Isoniazid, ethambutal and streptomycin were added to the regimen because of the documented exposure to tuberculosis two months previously.

Repeat lumbar puncture on day two showed an increase in protein level to 379 mg per 100 ml (Table 1). The patient continued to be lethargic and fever, nausea and vomiting were present. Findings on all routine cultures of blood and cerebrospinal fluid were negative, as were India ink and acid-fast bacilli stains and cytologic studies. Administration of ampicillin was discontinued, but antituberculous therapy was maintained. On day three the patient became afebrile, meningismus decreased and the cerebrospinal fluid level of protein declined. The patient improved symptomatically, and lumbar puncture on day five showed resolution of cerebrospinal fluid abnormalities.

On day six, viral cultures of cerebrospinal fluid obtained on day two showed cytopathic changes;

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herpesvirus hominis type 2 was subsequently isolated. Viral cultures of the genital lesions failed to grow herpesvirus, probably because the lesions had already crusted over. Unfortunately, no buffy coat cultures were obtained. Antituberculous medications were discontinued, and the patient was discharged. About one month after discharge, recrudescent meningismus and symptoms coincident with reappearance of labial herpetic lesions occurred. The patient refused lumbar puncture or labial lesion cultures and recovered without complication on bed rest alone. No further episodes have occurred. No oral or ocular lesions suggestive of Behçet's syndrome were ever evident.

Discussion

This case represents a culture-proved herpesvirus hominis type 2 meningitis. It is of interest because of the pronounced lymphocytosis and the very high protein levels in the cerebrospinal fluid and because of its association with herpes progenitalis infection. The initial symptom of sudden severe lumbarsacral spine pain is of interest in light of reports of ascending myelitis with herpes simplex virus (herpesvirus hominis type 1)[6] and the recent observations of Baringer[7] of herpesvirus hominis type 2 cultured from presacral ganglia of autopsied patients. One could speculate that the herpesvirus hominis type 2 in our patient traveled via the presacral ganglia to the central nervous system via a direct neural route rather than a hematogenous route as suggested by Craig and Nahmias.[2]

The genital lesions of our patient were treated with neutral red. Photodynamic inactivation of genital herpes infections with the heterotricyclic dyes proflavin or neutral red has been used as a therapeutic approach.[8-10] Recently, however, there has been some evidence to suggest that photodynamic inactivation may change the herpesvirus in such a way as to make it carcinogenic.[11] There is increasing reluctance to use photoinactivation therapy because of this evidence.

TABLE 1.—*Results of Analyses of Cerebrospinal Fluid Obtained by Serial Lumbar Punctures**

	Date 1974			
	10/13	10/14	10/15	10/17
	8 pm	1 am	2 pm	4 pm
Opening pressure mm Hg	273	150	230	180
Leukocytes				
Count/mm³	510	740	1,250	583
Polymorphonuclear (percent)	11	18	4	..
Lymphocytes (percent)	80	81	59	..
Eosinophils (percent)	5	1	1	..
Pia-arachnoid (percent)	..	..	34	..
Basophils (percent)	..	..	1	..
Red blood cells/mm³	60	80	400	42
Protein mg/100 ml	293	379	196	76
Glucose mg/100 ml	42	42	82	48
Blood	89	106	186	89
Cultures				
Routine	neg	neg	neg	neg
Acid-fast bacilli	neg	neg	neg	neg
Fungal	neg	neg	neg	neg
Viral	..	pos†	..	..

*In addition, findings on histoplasmin, cryptococcal and coccidioidomycosis complement fixation tests were all negative.
†Positive for herpesvirus hominis type 2.

Summary

Herpesvirus hominus type 2 was isolated from the cerebrospinal fluid of a woman with aseptic meningitis who recently had a herpes progenitalis infection. The meningitis was associated with an extremely high level of protein (379 mg per 100 ml) and extreme lymphocytosis in the cerebrospinal fluid.

ADDENDUM: Since the paper was submitted, the patient has had several recrudescences of the disease and has had to be admitted to hospital twice. On both of those occasions, cerebrospinal fluid, while showing moderate to minimal pleocytosis, normal sugar and normal protein, has been culture sterile for herpes type 2. During each exacerbation clinical features have been present compatible with a demyelinating disorder, including multifocal sensory and motor neurologic signs of both peripheral and cranial distribution. While there has been a definite temporal association between the recrudescence of the labial herpes and the meningitic, now encephalitic, episodes, it is not clear that we are dealing with an infectious process in relapse. Possibilities include an underlying demyelinating disorder or a postinfectious demyelinating syndrome which is unique in its resolution and relapse pattern. The patient currently is being treated with high doses of steroids and some clinical resolution is being seen.

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